PCT/DE2003/003988

Translation

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference P175802PC-La	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/DE2003/003988	International filing date (*day/month/year*) 28 November 2003 (28.11.2003)	Priority date (*day/month/year*) 29 November 2002 (29.11.2002)
International Patent Classification (IPC) or national classification and IPC G01N 33/564		
Applicant MAX-DELBRÜCK-CENTRUM FÜR MOLEKULARE MEDIZIN		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 7 sheets, including this cover sheet.

   ☒ This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of 13 sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the report
   - II ☐ Priority
   - III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - VI ☐ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☐ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
28 June 2004 (28.06.2004)	31 January 2005 (31.01.2005)
Name and mailing address of the IPEA/EP Facsimile No.	Authorized officer Telephone No.

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/DE2003/003988

I. Basis of the report

1. This report has been drawn on the basis of (*Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to the report since they do not contain amendments.*):

☐ the international application as originally filed.

☒ the description, pages 1-42, as originally filed,
pages _____, filed with the demand,
pages _____, filed with the letter of _____,
pages _____, filed with the letter of _____.

☒ the claims, Nos. _____, as originally filed,
Nos. _____, as amended under Article 19,
Nos. _____, filed with the demand,
Nos. 1-31, filed with the letter of 17 December 2004 (17.12.2004),
Nos. _____, filed with the letter of _____.

☒ the drawings, sheets/fig 1/1, as originally filed,
sheets/fig _____, filed with the demand,
sheets/fig _____, filed with the letter of _____,
sheets/fig _____, filed with the letter of _____.

2. The amendments have resulted in the cancellation of:

☐ the description, pages _____
☐ the claims, Nos. _____
☐ the drawings, sheets/fig _____

3. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).

4. Additional observations, if necessary:

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
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III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application.

☒ claims Nos. 12, 16 (partially), 30, 31 (industrial applicability)

because:

☒ the said international application, or the said claims Nos. 12, 16 (partially)
relate to the following subject matter which does not require an international preliminary examination *(specify)*:

☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. _____
are so unclear that no meaningful opinion could be formed *(specify)*:

☐ the claims, or said claims Nos. _____ are so inadequately supported
by the description that no meaningful opinion could be formed.

☒ no international search report has been established for said claims Nos. 30, 31 (industrial applicability).

Supplemental Box
(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of: Box III.

Claims 30 and 31 relate to a subject matter which in the view of this Authority falls within the scope of PCT Rule 67.1(iv). Therefore, no opinion is established regarding the industrial applicability of the subject matter of these claims (PCT Article 34(a)(i)).

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims	1-31	YES
	Claims		NO
Inventive step (IS)	Claims	1-31	YES
	Claims		NO
Industrial applicability (IA)	Claims	1-31	YES
	Claims		NO

2. Citations and explanations

1. Novelty

The subject matter of claims 1-31, insofar as it concerns peptides used to detect autoantibodies that are associated with Raynaud syndrome (see also **Certain Defects** below), said autoantibodies being directed against peptides of G protein-coupled receptors PAR-1, PAR-2, PAR-3 and/or endothelin IA, is novel within the meaning of PCT Article 33(2) because said antibodies have not been described in the prior art.

2. Inventive step

Claims 1-31 are considered inventive within the meaning of PCT Article 33(3).
In the prior art it is known that Raynaud syndrome can be linked with the presence of autoantibodies. Thus, the document BOROS PETER ET AL.: "Specificity and class distribution of Fc-gamma-R-specific autoantibodies in patients with autoimmune disease", JOURNAL OF IMMUNOLOGY, THE WILLIAMS AND WILKINS CO., BALTIMORE, US, Vol. 152, 1994, pages 302-306 (D5), discloses that autoantibodies directed against Fc-

gamma-RIII can be detected in the serum of patients with Raynaud syndrome (see the abstract).
MACFARLANE S R ET AL.: "Proteinase-activated receptors", PHARMACOLOGICAL REVIEWS, WILLIAMS AND WILKINS INC., BALTIMORE, MD, US, Vol. 53, No. 2, June 2001 (2001-06), pages 245-282 (D6) discusses a possible role of anticentromer antibodies in the Raynaud phenomenon (see the passages cited in the search report).
However, neither D5 nor D6 discloses or suggests that autoantibodies directed against peptides of G protein-coupled receptors PAR-1, PAR-2 or endothelin IA play a role in the Raynaud syndrome.
Claims 1-31 can therefore be considered inventive within the meaning of PCT Article 33(3).

Certain Defects in the International Application

The present international Preliminary Examination Report relates only to the part of the application that refers to the Raynaud syndrome.
The applicant has not paid additional search fees for the inventions 2-10 indicated in the international search report. Hence, under PCT Rule 66.1(e), inventions 2-10 are not covered by the international preliminary examination. Moreover, in the applicant's letter of December 17, 2004, the applicant has expressly requested only the examination of invention 11. Peptides that are not associated with invention 11 are thus not covered by the international preliminary examination. These remarks are relevant primarily to the subject matter of claims 12 and 16.

Certain Observations on the International Application

Independent claim 1 relates to a method of detecting

disease-related autoantibodies that are directed against G protein-coupled receptors and associated with Raynaud syndrome, which method includes the use of peptides from loops of said receptors.

The description provides support and/or sufficient disclosure for only a limited number of said receptors that are associated with the Raynaud syndrome, namely PAR-1, PAR-2, PAR-3 and endothelin IA.

With the definition of "G protein-coupled receptors that are associated with the Raynaud syndrome" the application attempts to define the subject matter by the result to be achieved; however, that merely indicates the problem to be solved without providing the technical features necessary for achieving this result. Claim 1 thus does not meet the requirements of PCT Article 5 and 6.